王老师好，

根据组会上的几点修改意见进行了相应修改。 增加了相应的图标及文字。麻烦王老师趁着组会的印象还没消去，对文章进行一次文字方面的修改吧。

Shicheng

1. **抽提文章中Ad2Sc的信息，然后进行亚组分析，结果发现Ad2Sc > 1和 < 1的两个压组，OR没有显著性差异。（原因解释如下第三部分）**

1. **把所有引物找出来， 发现17篇文章共采用了3套引物：**

type A: 7篇,

type B: 7篇

type C：1篇，

其余文章引物无法定位或者没有提供引物信息）

**Supplementary Table 5, Five kinds of primers of 17 studies**

|  |  |  |  |
| --- | --- | --- | --- |
| Study | Forward | Reverse | Type |
| Pan et al (2009,China) | ACTGCCATCAACTTCCTTGCTTGCT\* | GACATGTGGCTGTATTGGTGCAGCCCG | chr5:112073311-112073571 |
| Zhang et al (2011,China)b | CACTGCGGAGTGCGGGTC | CCGTCGGGAGCCCGCCGA | chr5:112073421+112073518 |
| Virmani et al (2001, USA) | CACTGCGGAGTGCGGGTC | CCGTCGGGAGCCCGCCGA | chr5:112073421+112073518 |
| Kim et al (2007, Korea) | CACTGCGGAGTGCGGGTC | CCGTCGGGAGCCCGCCGA | chr5:112073421+112073518 |
| Lin et al (2009, China) | CACTGCGGAGTGCGGGTC | CCGTCGGGAGCCCGCCGA | chr5:112073421+112073518 |
| Shivapurkar et al (2007, USA) | CACTGCGGAGTGCGGGTC | CCGTCGGGAGCCCGCCGA | chr5:112073421+112073518 |
| Suzuki et al (2006, Japan) | CACTGCGGAGTGCGGGTC | CCGTCGGGAGCCCGCCGA | chr5:112073421+112073518 |
| Zhang et al (2011, China)b | CACTGCGGAGTGCGGGTC | CCGTCGGGAGCCCGCCGA | chr5:112073421+112073518 |
| Rykova et al (2004, Russia) | CACTGCGGAGTGCGGGTC | CCGTCGGGAGCCCGCCGA | chr5:112073421+112073518 |
| **Begum et al (2011, USA)** | **GGACCAGGGCGCTCCCCAT** | **GTGTGGGCGCACGTGACCGACATGTGG** | **chr5:112101379+112101452** |
| **Usadel et al (2002, USA)** | **GGACCAGGGCGCTCCCCAT** | **GTGTGGGCGCACGTGACCGACATGTGG** | **chr5:112101379+112101452** |
| **Jin et al (2009, Japan)** | **GGACCAGGGCGCTCCCCAT** | **GTGTGGGCGCACGTGACCGACATGTGG** | **chr5:112101379+112101452** |
| **Feng et al (2008, USA)** | **GGACCAGGGCGCTCCCCAT** | **GTGTGGGCGCACGTGACCGACATGTGG** | **chr5:112101379+112101452** |
| **Brabender et al (2001, USA)** | **GGACCAGGGCGCTCCCCAT** | **GTGTGGGCGCACGTGACCGACATGTGG** | **chr5:112101379+112101452** |
| **Vallbohmer et al (2006, USA)** | **GGACCAGGGCGCTCCCCAT** | **GTGTGGGCGCACGTGACCGACATGTGG** | **chr5:112101379+112101452** |

The primers of the study of Wang et al (2008, China), Topaloglu et al (2004, USA) and Yanagawa et al (2003, Japan) can't be located.

1. **然后和芯片上的6个点进行比较，这6个点和所有primer都没有重叠。但cg20311501位于type B primer的扩增区域（supplementary table 1 and table 5）。 这个cg20311501在Ad和SC中都是显著差异的位点(table 4)，所以可能是这个原因，导致meta分析中无法发现Ad2Sc是异质性来源。**

**Supplementary Table 1 TCGA probe information in this study**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| CpG ID | Chrosome | MapInfo | Strand | Accession | Distance to TSS | CpG Island |
| cg01240931 | Chr5 | 112101942 | + | NM\_000038.3 | -459 | FALSE |
| cg15020645 | Chr5 | 112101668 | + | NM\_000038.3 | -185 | FALSE |
| cg16970232 | Chr5 | 112101332 | + | NT\_034772.5 | 151 | TRUE |
| cg20311501 | Chr5 | 112101401 | + | NT\_034772.5 | 82 | TRUE |
| cg21634602 | Chr5 | 112101469 | + | NM\_000038.3 | 14 | TRUE |
| cg24332422 | Chr5 | 112101585 | + | NM\_000038.3 | -102 | TRUE |

**Table 4**, Differential APC methylation status (Beta) between adenocarcinoma, squamous cell carcinoma and its counterparts based on t-test

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Adenocarcinoma | | | | Squamous Cell Carcinoma | | | |
| CpG Site | MCoM  (N=535) | MCoM  (N=56) | P-value | FDR | MCaM  (N=386) | MCoM  (N=70) | P-value | FDR |
| cg01240931 | 0.54(96.45%) | 0.47(100%) | 1.91×10-10 | **1.91×10-10** | 0.4(75.39%) | 0.44(100%) | 0.000178 | **0.000535** |
| cg15020645 | 0.26(40.75%) | 0.13(0%) | 3.54×10-32 | **1.06×10-31** | 0.13(14.77%) | 0.11(0%) | 0.087466 | 0.131199 |
| cg16970232 | 0.3(45.23%) | 0.11(0%) | 5.03×10-38 | **3.02×10-37** | 0.15(18.91%) | 0.09(0%) | 2.7×10-7 | **1.6×10-6** |
| cg20311501 | 0.33(48.41%) | 0.16(5.36%) | 1.40×10-22 | **2.10×10-22** | 0.18(19.95%) | 0.14(0%) | 0.001955 | **0.003909** |
| cg21634602 | 0.33(47.48%) | 0.16(7.14%) | 3.63×10-17 | **4.36×10-17** | 0.16(20.47%) | 0.14(7.14%) | 0.222306 | 0.266767 |
| cg24332422 | 0.26(40.56%) | 0.16(0%) | 1.01×10-26 | **2.02×10-26** | 0.16(17.36%) | 0.15(0%) | 0.338755 | 0.338755 |

1. **SROC部分和Pca的比较全部移至discussion部分**